Complete Summary

GUIDELINE TITLE

The role of neoadjuvant chemotherapy in locally advanced squamous cell carcinoma of the head and neck (SCCHN) (excluding nasopharynx).

BIBLIOGRAPHIC SOURCE(S)

Head and Neck Cancer Disease Site Group. Browman GP, Hodson DI, Newman T. The role of neoadjuvant chemotherapy in locally advanced squamous cell carcinoma of the head and neck (SCCHN) (excluding nasopharynx) [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2003 Feb [online update]. 10 p. (Practice guideline; no. 5-1). [36 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Locally advanced squamous cell carcinoma of the head and neck (SCCHN) (excluding nasopharynx)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Internal Medicine
Oncology
Radiation Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To determine if the addition of neoadjuvant chemotherapy to conventional local treatment with radiation and/or surgery is effective in improving survival in patients with locally advanced squamous cell head and neck cancer compared with conventional therapy alone

TARGET POPULATION

Adult patients with locally advanced squamous cell carcinoma of the head and neck (excluding nasopharynx)

INTERVENTIONS AND PRACTICES CONSIDERED

1. Neoadjuvant chemotherapy
2. Neoadjuvant chemotherapy in combination with radiation therapy

MAJOR OUTCOMES CONSIDERED

Overall survival is the primary outcome of interest. Quality of life (preservation of organ function) is also considered.

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

1996 Guideline
A MEDLINE search was done for the years 1980 to June 1994 using the subject headings "head and neck neoplasms and (chemotherapy or neoadjuvant or adjuvant)" and "randomized controlled trials". Abstracts were excluded from consideration in the original report of December 1994. The same search terms were used when this guideline was updated in February 1996. "Meta-analysis" and "clinical trials" were added as publication types. A CANCERLIT database search was also done. Abstracts published in 1994 and 1995 were included because of empirical evidence suggesting serious biases favoring experimental treatments where systematic reviews excluded abstracts. The citation lists of all retrieved articles were further searched to identify additional studies. The search was restricted to English language publications.

2003 Update
The literature was searched using MEDLINE (through January 2003), CANCERLIT (through October 2002), the Cochrane Library (Issue 4 2002), the Physician Data

Query (PDQ) database, clinical trial and practice guideline Internet sites, abstracts published in the proceedings of the annual meetings of the American Society of Clinical Oncology (1999-2002), the American Society for Therapeutic Radiology and Oncology (1999-2002) and the European Society for Medical Oncology (1998, 2000). Article bibliographies and personal files were also searched to November 2002.

Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence if they met the following criteria:

1. Randomized controlled trials of neoadjuvant chemotherapy prior to local treatment with conventional radiation and/or surgery versus local treatment alone as the control.
2. Abstracts published in 1994 or later were included if the data could be extracted for analysis.

Exclusion Criteria

Trials were excluded if they concerned recurrent or metastatic disease, patients had been previously treated, nasopharynx cancer was an important fraction of the population studied, chemotherapy was not the first modality used, the control arm did not use conventional radiotherapy with or without surgery, chemotherapy was used either with alternating or concurrently with radiation, intra-arterial chemotherapy was used, or publications did not present data in an analyzable form.

NUMBER OF SOURCE DOCUMENTS

1996 Guideline

The 1994 report included 12 trials. Seven further trials of neoadjuvant chemotherapy and an additional four trials for the subgroup analysis of neoadjuvant plus adjuvant therapy were reviewed.

2003 Update

The updated literature search identified three published meta-analyses and twelve new or updated randomized trials that met the inclusion criteria. In addition, a follow-up study of quality-of-life data from a randomized trial cited in the earlier report was located.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Randomized Controlled Trials
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

This guideline report was developed by the Practice Guidelines Initiative (PGI), using the methodology of the Practice Guidelines Development Cycle (see companion document by Browman et al). Evidence was selected and reviewed by one member of the Practice Guidelines Initiative Head and Neck Cancer Disease Site Group (DSG) and methodologists.

1996 Guideline

To estimate the overall effect on survival of neoadjuvant chemotherapy versus conventional local therapy, the results of the randomized trials using meta-analysis were pooled according to software provided by Dr. Joseph Lau, Tufts New England Medical Center, Boston, MA. Results are expressed as the odds ratio with 95% confidence intervals (CI) such that estimates >1.0 favor control and estimates <1.0 favor neoadjuvant chemotherapy. Data were analyzed using both fixed-effect (Mantel-Haenszel) and random effect models. The results were similar and those of the random effects model are shown in the guideline document. Finally, a subgroup analysis was performed to determine whether the addition of adjuvant chemotherapy to neoadjuvant therapy was beneficial, and to determine whether neoadjuvant trials employing the combination of cisplatinum and infusional 5-fluorouracil (CP-FU) were beneficial.

The previous report (December 1994) combined the results of trials in the meta-analysis by selecting a common follow-up period across studies. For the current version, a constant odds ratio over time has been assumed to allow for a longer follow-up period in each trial. The follow-up time was restricted to a point at which at least 50% of patients had been followed (median follow-up). The assumption of constant odds ratio is sufficiently robust for the purposes of this analysis. The analytic method overestimates the precision of the confidence limits because the denominators used in the analyses were based on patients randomized, which is higher than the number of patients at risk for the period of follow-up. This should not affect the point estimates themselves, and in light of the overall results this overestimation of precision does not alter the conclusions.

2003 Update

With the recent publication of a pooled analysis using individual patient data, new studies were not added to the original meta-analysis.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

There was a general consensus among Disease Site Group (DSG) members about the main thrust of this recommendation. Areas of discussion in the previous report

included: 1) the potential uses of cause-specific survival as opposed to overall survival as the appropriate outcome; and 2) whether patients with advanced resectable larynx cancer should be advised of the results of the Veterans Administration trial for the purpose of shared decision making. The DSG members felt that: 1) for treatment purposes, overall survival is the most appropriate outcome on which to base decisions at this time; 2) the lack of a radiation alone control arm in the Veterans Administration study is sufficiently serious to preclude a recommendation for offering patients with resectable larynx cancer the option of an organ preservation strategy that includes chemotherapy; however, the DSG members remained split on this issue, with some advocating full information being given to patients for shared decision making.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

1996 Guideline

Practitioner feedback was obtained through a mailed survey of 63 practitioners in Ontario. The survey consisted of items evaluating the methods, results and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The results of the survey were reviewed by the Head and Neck Cancer Disease Site Group. The guidelines have been approved by the Head and Neck Cancer Disease Site Group and the Practice Guideline Coordinating Committee.

2003 Update

The new information from review and updating activities was not subject to external review because the new evidence is consistent with the data used to inform the original guideline.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Neoadjuvant chemotherapy should not be used in the routine management of patients with locally advanced squamous cell carcinoma of the head and neck if the main objective is improved survival.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

1996 Guideline
High quality evidence (randomized controlled trials and meta-analyses of trials) was available for review. The previous report (December, 1994) included 12 trials. Seven further trials of neoadjuvant chemotherapy and an additional four trials for the subgroup analysis of neoadjuvant plus adjuvant therapy were added. Some trials were published before 1994 but were missed in the literature search for the previous version of this guideline.

2003 Update
The updated literature search identified three published meta-analyses and twelve new or updated randomized trials that met the inclusion criteria. In addition, a follow-up study of quality-of-life data from a randomized trial cited in the 1996 guideline was located.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

A meta-analysis using individual patient data from 31 randomized trials (5269 patients) demonstrated no significant survival benefit for neoadjuvant chemotherapy compared with locoregional treatment alone (hazard ratio, 0.95; 95% CI, 0.88 to 1.01; p=0.10). However, a subgroup analysis of 15 trials (2487 patients) detected significantly improved survival with neoadjuvant chemotherapy using fluorouracil plus either cisplatin or carboplatin (hazard ratio, 0.88; 95% CI, 0.79 to 0.97; p<0.05). Individual patient data from three trials of larynx-preservation versus surgery were pooled in a separate analysis (602 patients). The hazard ratio for death was not-significant in favour of surgery over larynx preservation (HR = 1.19, 95% CI, 0.97 to 1.46; p=0.10) favoring surgery.

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

1996 Guideline
Not stated

2003 Update

Since the initial release of this guideline, it has become common practice to use neoadjuvant chemotherapy in a combined modality approach with radiation to preserve organ function to achieve enhanced quality of life in patients with otherwise resectable disease. The randomized trials demonstrate that when neoadjuvant chemotherapy is combined with radiotherapy, organ function can be preserved in a substantial proportion of otherwise resectable patients with improved quality of life. However, there is a trend for reduced survival which is not significant. Preliminary results from a large organ preservation trial indicate that with no differences in overall survival, neoadjuvant chemotherapy with radiotherapy produces similar outcomes as radiotherapy alone. Neither treatment was as effective as concomitant chemotherapy and radiation in terms of laryngectomy preservation rate and loco-regional control.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Head and Neck Cancer Disease Site Group. Browman GP, Hodson DI, Newman T. The role of neoadjuvant chemotherapy in locally advanced squamous cell carcinoma of the head and neck (SCCHN) (excluding nasopharynx) [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2003 Feb [online update]. 10 p. (Practice guideline; no. 5-1). [36 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 Feb 15 (updated online 2003 Feb)

GUIDELINE DEVELOPER(S)

Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario, Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Head and Neck Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Head and Neck Cancer Disease Site Group disclosed potential conflict of interest information.

GUIDELINE STATUS

This is the current release of the guideline.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web site for details on any new evidence that has emerged and implications to the guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Neoadjuvant chemotherapy in locally advanced squamous cell carcinoma of the head and neck (SCCHN) (excluding nasopharynx). Summary. Toronto

(ON): Cancer Care Ontario. Electronic copies: Available in portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on August 19, 1999. The information was verified by the guideline developer as of September 17, 1999. This summary was updated by ECRI on December 3, 2001 and most recently on July 21, 2003. The most recent information was verified by the guideline developer as of August 6, 2003.

COPYRIGHT STATEMENT

Date Modified: 11/15/2004